WO 2005/085194 PCT/GB2005/000872

CLAIMS:

1. A compound of formula (I):

or a pharmaceutically acceptable salt thereof, wherein:

Y is -C(O)-, $-S(O)_2$ -, or -C(NH)-;

Z is C_{1-4} alkylene, oxygen, $-(CH_2)_mO$ -, $-O(CH_2)_m$ -, -NR-, $-(CH_2)_mNR$ -, $-NR(CH_2)_m$ -, $-(CH_2)_mS(O)_2$ -, or a bond;

m is 1, 2, 3, or 4;

R is C_{0-4} alkyl, C_{0-4} alkylaryl, or C_{0-4} alkylheoaryl;

R¹ and R¹ are each independently, halogen, hydroxy, cyano, C₀₋₄alkyl, C₁₋₄alkoxy, fluoromethyl, difluoromethyl, trifluoromethyl, ethenyl, or ethynyl;

R² is C_{0.4}alkyl, COOR⁶, COR⁶, C_{1.4}alkoxyC_{1.4}alkyl–, hydroxyC_{1.4}alkyl–, cycloalkylC_{0.4}alkyl–, arylC_{0.4}alkyl–, or hetarylC_{0.4}alkyl–, wherein any of the aryl or hetaryl rings are optionally substituted with 1-2 independent halogen, cyano, C_{1.4}alkyl, C_{1.4}alkoxy, –N(C_{0.4}alkyl)(C_{0.4}alkyl), –SO₂C_{1.4}alkyl, –SO₂N(C_{0.4}alkyl)(C_{0.4}alkyl), hydroxy, fluoromethyl, difluoromethyl, or trifluoromethyl substituents;

 R^3 is hydrogen, $-COOC_{0.4}$ alkyl, $C_{1.4}$ alkoxy, $C_{1.4}$ alkyl, aryl $C_{1.4}$ alkylthio-, $-C_{0.4}$ alkylaryl, $-C_{0.4}$ alkyletaryl, $-C_{0.4}$ alkylcycloalkyl, or $-C_{0.4}$ alkylheterocyclyl, wherein any of the rings is optionally substituted with 1-3 independent halogen, cyano, $C_{1.4}$ alkyl, fluoromethyl, difluoromethyl, trifluoromethyl, $-C_{0.4}$ alkylNHC(O)O($C_{1.4}$ alkyl), $-C_{0.4}$ alkylNR 7 R 8 , -C(O)R 9 , $C_{1.4}$ alkoxy $C_{0.4}$ alkyl-, $-COOC_{0.4}$ alkyl, $-C_{0.4}$ alkylNHC(O)R 9 , $-C_{0.4}$ alkylC(O)N(R 10)₂, $-C_{1.4}$ alkoxy $C_{1.4}$ alkoxy, hydroxy $C_{0.4}$ alkyl-, $-NHSO_2R^{10}$, $-SO_2(C_{1.4}$ alkyl), $-SO_2NR^{11}R^{12}$, 5- to 6-membered heterocyclyl, phenyl $C_{0.2}$ alkoxy, or phenyl $C_{0.2}$ alkyl substituents, wherein phenyl is optionally substituted with 1-2 independent halogen, cyano, $C_{1.4}$ alkyl, $C_{1.4}$ alkoxy, $-N(C_{0.4}$ alkyl)($C_{0.4}$ alkyl), $-SO_2C_{1.4}$ alkyl, $-SO_2N(C_{0.4}$ alkyl)($C_{0.4}$ alkyl), hydroxy, fluoromethyl, difluoromethyl, or trifluoromethyl substituents, or two bonds on a ring carbon of the heterocyclyl group optionally can form an oxo (=O) substituent;

or R^3 is $-NR^4(-C_{0.4}alkylR^5)$;

 R^4 is C_{0-3} alkyl, $-C_{2-3}$ alkyl- NR^7R^8 , C_{3-6} cycloalkyl optionally substituted by hydroxy C_{0-4} alkyl- further optionally substituted by hydroxy, C_{1-2} alkoxy C_{2-4} alkyl-, or C_{1-2} alkyl- $S(O)_n$ - C_{2-3} alkyl-;

n is 0, 1, or 2;

 R^5 is hydrogen, hydroxy $C_{2\text{--}3}$ alkyl-, $C_{1\text{--}2}$ alkoxy $C_{0\text{--}4}$ alkyl-, or aryl, hetaryl, or heterocyclyl;

wherein a heterocyclic nitrogen-containing R^5 ring optionally is mono-substituted on the ring nitrogen with C_{1-4} alkyl, benzyl, benzyl, C_{1-4} alkyl-C(O)–, $-SO_2C_{1-4}$ alkyl, $-SO_2N(C_0$ - $_4$ alkyl), C_{1-4} alkoxycarbonyl, or aryl(C_{1-4} alkoxy)carbonyl; and wherein the R^5 rings are

WO 2005/085194 PCT/GB2005/000872

optionally mono-substituted on a ring carbon with halogen, cyano, C_{1-4} alkyl-C(O)-, C_{1-4} alkyl- SO_2 -, C_{1-4} alkyl, C_{1-4} alkyl, C_{1-4} alkyl, C_{1-4} alkyl, C_{1-4} alkyl-, or C_{0-4} alkyl), hydroxy C_{0-4} alkyl-, or C_{0-4} alkylcarbamoyl-, provided that no quaternised nitrogen is included; or two bonds on a ring carbon of the heterocycle optionally can form an oxo (=O) substituent;

R⁶ is C_{1.4}alkyl, aryl, or hetaryl;

R⁷ and R⁸ are independently C_{0.4}alkyl, C_{3.6}cycloalkyl, or CO(C_{1.4}alkyl);

R⁹ is C₁₋₄alkyl, or C₃₋₆cycloalkyl;

R¹⁰ is C₀₋₄alkyl, or C₃₋₆cycloalkyl; and

R¹¹ and R¹² are independently C₀₋₄alkyl or together with the nitrogen to which they are attached may form a 4- to 6-membered heterocycle;

provided there are no nitrogen-oxygen, nitrogen-nitrogen, oxygen-oxygen or nitrogen-halogen bonds in the grouping -Y-Z-R³; and

provided that when -Y-Z- represents -C(O)-, -C(NH)-, -C(O)- C_{1-4} alkylene, -C(NH)- C_{1-4} alkylene, -C(O)-NR-, -C(NH)-NR-, -C(O)-(CH₂)_mNR-, or -C(NH)-(CH₂)_mNR-, then R³ is not optionally substituted C_{3-10} cycloalkyl, C_{5-10} cycloalkenyl, phenyl, naphthyl, pyridyl, pyrazinyl, pyrazolyl, imidazolyl, triazolyl, thiazolyl, furanyl, thiophenyl, pyrrolyl, pyrrolyl, piperidinyl, indolyl, benzo[1,3]dioxol, thieno[2,3-b]pyrrolyl, or thieno[3,2-b]pyrrolyl.

- 2. A compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein Y is -C(O)- or -S(O)₂-.
- 3. A compound according to claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein Z is C_{1-4} alkylene, oxygen, $-(CH_2)_mO$ -, -NR- or a bond.
- 4. A compound according to any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein Y is -C(O)-.
- 5. A compound according to any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein Y is -S(O)₂-.
- 6. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^1 and $R^{1'}$ are each independently, hydrogen or halogen.
- 7. A compound according to claim 4, or a pharmaceutically acceptable salt thereof, wherein one of R^1 and R^1 is hydrogen and the other is 5-chloro.
- 8. A compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof, wherein R^2 is hydrogen.
- 9. A compound of formula (I) as defined in any one of Examples 1 to 41, or a pharmaceutically acceptable salt thereof.

WO 2005/085194 PCT/GB2005/000872

10. A pharmaceutical composition comprising a compound according to any one of the preceding claims, or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable carrier.

- 11. A method for the treatment of a disease or condition in which glycogen phosphorylase plays a role comprising a step of administering to a subject in need thereof an effective amount of a compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof.
- 12. A method for the treatment of hyperglycemia or diabetes comprising a step of administering to a subject in need thereof an effective amount of a compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof.
- 13. A method for the prevention of diabetes in a human demonstrating pre-diabetic hyperglycemia or impaired glucose tolerance comprising a step of administering to a subject in need thereof an effective prophylactic amount of a compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof.
- 14. A method for the treatment of hypercholesterolemia, hyperinsulinemia, hyperlipidemia, hypertension, atherosclerosis or tissue ischemia, or achieving cardioprotection or inhibition of abnormal cell growth, comprising a step of administering to a subject in need thereof an effective amount of a compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof.